

REMARKS/ARGUMENTS

The Pending Claims

Claims 1-16 are pending and are directed to a method of producing pluripotent stem cells.

Amendments to the Claims

The claims have been amended to point out more particularly and claim more distinctly the invention. In particular, claim 1 has been amended to clarify that the testis cells contain spermatogonial stem cells and to include the step of isolating pluripotent stem cells from the cultured testis cells. The amendments to claim 1 are supported by the specification at, for example, page 13, lines 17-22; page 14, lines 23-28; and page 25, line 33, through page 26, line 6.

Claims 17-34 have been canceled inasmuch as these claims are drawn to non-elected subject matter.

No new matter has been added by way of the amendments to the claims.

Amendments to the Specification

The amendment to the specification set forth in the Preliminary Amendment dated September 29, 2006, has been resubmitted with the correct page and line numbers.

No new matter has been added by way of the amendment to the specification.

Summary of the Office Action

The Office maintains the restriction requirement and withdraws claims 17-34 from consideration.

The Office indicates that the amendment to the specification set forth in the Preliminary Amendment dated September 29, 2006, has not been entered because the wrong page and line numbers were indicated.

The Office rejects claims 1-6 under 35 U.S.C. § 102(b) as allegedly anticipated by Nagano et al., *Biology of Reproduction*, 68: 2207-2214 (2003).

The Office rejects claims 8-16 under 35 U.S.C. § 102(a) as allegedly anticipated by Kubota et al., *PNAS*, 101(47): 16489-16494 (2004)).

The Office rejects claims 1-16 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement.

The Office provisionally rejects claims 1-6 on the grounds of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 1-7 and 12 of co-pending U.S. Patent Application No. 10/553,118.

Reconsideration of the rejections is hereby requested.

Information Disclosure Statements

Applicants filed two Information Disclosure Statements dated January 2, 2007, and July 11, 2007. The Information Disclosure Statements were accompanied by Forms PTO-1449, which identified references AA-AL. The Office Action Summary indicates that the Forms PTO-1449 were attached to the Office Action (see page 1 of the Office Action); however, the forms were not attached. Applicants respectfully request entry of the Information Disclosure Statements and return of a copy of the Examiner-initialed Forms PTO-1449, thereby confirming the Examiner's consideration of references AA-AL.

Discussion of the Anticipation Rejections

The anticipation rejections are traversed for the following reasons.

A. Nagano et al.

The Office contends that Nagano et al. teaches culturing testis cells from transgenic mice using a medium containing GDNF to obtain pluripotent stem cells. However, Nagano et al. only discloses a method of expanding spermatogonial stem cells and does *not* disclose the production of pluripotent stem cells, as required by the pending claims. Spermatogonial stem cells and pluripotent stem cells derived from testis cells differ substantially in their

properties (see, e.g., page 25, lines 22-32, and page 28, line 31, through page 32, line 9, of the specification).

The pending claims, as amended, recite a step of isolating pluripotent stem cells from cultured testis cells. It is only by recognizing the presence of such pluripotent stem cells in the cultured testis cells that one could perform the claimed method. Nagano et al. does not disclose the presence of pluripotent stem cells, let alone disclose the isolation of the pluripotent stem cells. Therefore, Nagano et al. cannot be considered to anticipate the pending claims, and the anticipation rejection based on Nagano et al. should be withdrawn.

B. Kubota et al.

The Office contends that claims 8-16 are anticipated by Kubota et al. Kubota et al. published online on November 1, 2004, which is after the filing date of Japanese Patent Application No. 2004-101320 (i.e., March 30, 2004), to which the current application claims priority. The Japanese priority document contains support for claims 8-16, as evidenced by the English translation submitted herewith (see, e.g., page 5, lines 1-17; and page 6, line 20, through page 7, line 13). Accordingly, Kubota et al. is not prior art to claims 8-16, and the anticipation rejection based on Kubota et al. should be withdrawn.

Discussion of the Enablement Rejection

The Office contends that the specification lacks enablement for the subject matter of claims 1-16. Applicants traverse this rejection for the following reasons.

The Office contends that the specification does not provide guidance for producing pluripotent stem cells from testis by forming all three somatic lineages (i.e., endoderm, ectoderm, and mesoderm). However, the specification describes the formation of a variety of cell types from the pluripotent stem cells using protocols for ES cell differentiation (see, e.g., page 56, line 17, through page 59, line 21). The specification also describes the formation of teratomas containing cells of the three somatic lineages (see, e.g., page 59, line 12, through page 60, line 25). Additionally, the specification describes the generation of chimeric animals and offspring derived from the pluripotent stem cells, wherein the pluripotent stem cells resulted in cells of central nervous system, liver, heart, lung, testis, somites, intestine, and other tissues (see, e.g., page 60, line 26, through page 61, line 31). Furthermore, the

specification describes the formation of a fetus derived from the pluripotent stem cells by tetraploid complementation assay (see, e.g., page 62, lines 8-20).

Accordingly, the specification provides evidence that the pluripotent stem cells are capable of differentiating into somatic cells from the three different lineages (i.e., ectoderm, endoderm, and mesoderm), as well as germline cells (see, e.g., page 62, lines 21-24).

The Office also contends that the specification does not provide guidance for the production of pluripotent cells from the testis cells of all species. Although the specification provides examples of the claimed method using testis cells from mice, one of ordinary skill in the art would have recognized that the claimed methods could be successfully employed using the testis cells from other animals, such as rats. The specification describes that the claimed method can be used with testis cells from any animal, such as a mammal (e.g., a mouse, rat, hamster, guinea pig, rabbit, pig, cow, goat, horse, sheep, dog, cat, and primate) (see, e.g., page 15, lines 6-21). This is supported by Brons et al., *Nature*, 448: 191-195 (2007) (a copy of which is submitted herewith), which describes that EpiSCs, which are a type of pluripotent cell, can be established from mouse and rat epiblasts using the same conditions that are sufficient for long-term maintenance of human embryonic stem cells (see Abstract, as well as Methods on page 194).

Accordingly, based on the description in the specification (which is supported by the state of the post-filing art), one of ordinary skill in the art would have understood how to make and use the claimed method with testis cells from animals other than mice with a reasonable expectation of success.

The Office additionally contends that the specification does not provide guidance for the production of pluripotent stem cells from fully differentiated cells (e.g., epithelial cells or fibroblasts). The claims have been amended to recite that the testis cells contain spermatogonial stem cells, as described in the specification (see, e.g., page 13, lines 17-22). This amendment to the claims is believed to address the Office's concerns.

Furthermore, the Office contends that the specification is only enabling for a method using a medium containing GDNF, LIF, and bFGF. The specification describes a medium containing GDNF or an equivalent thereto for use in the claimed method. The specification

indicates that a medium containing GDNF, LIF, and bFGF is only one embodiment for use in the claimed method. Applicants note that growth factors, such as LIF and FGF, are commonly used for the establishment of pluripotent stem cells (see Table 1 of Rossant, *Cell*, 132: 527-531 (2008); a copy of which is submitted herewith). Thus, even if the claims do not recite these particular growth factors, one of ordinary skill in the art would have recognized that the growth factors could be added to the medium based on the teachings in the specification and the technical knowledge regarding the art of pluripotent stem cells. Accordingly, one of ordinary skill in the art would have understood how to make and use the claimed invention with a reasonable expectation of success.

For the above-described reasons, the pending claims are fully enabled by the specification and the enablement rejection should be withdrawn.

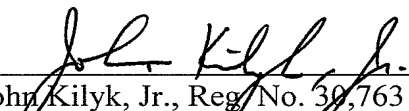
Discussion of the Provisional Nonstatutory Obviousness-Type Double Patenting Rejection

The Office contends that claims 1-6 are unpatentable over claims 1-7 and 12 of U.S. Patent Application No. 10/553,118. Due to the *provisional* nature of this rejection, Applicants will address the rejection at which time the application issues and the rejection becomes non-provisional.

Conclusion

Applicants respectfully submit that the patent application is in condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,



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